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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,195	10/31/2003	Linda M. Pacioretty	CLANACCR_001NP	4532

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EXAMINER	
CHONG, YONG SOO	
ART UNIT	PAPER NUMBER
1627	

MAIL DATE	DELIVERY MODE
12/08/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/699,195	PACIORETTY ET AL.	
	Examiner	Art Unit	
	Yong S. Chong	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *1-20,25-27,30,31 and 36-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-24, 28-29, 32-35, 39-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

This Office Action is in response to applicant's arguments filed on 8/18/09. Claim(s) 1-40 are pending. Claim(s) 21 and 32 have been amended. Claim(s) 1-20, 25-27, 30-31, 36-38 have been withdrawn. Claim(s) 21-24, 28-29, 32-35, 39-40 are examined herein.

The terminal disclaimer filed on 10/27/08 disclaiming the terminal portion of any patent granted on this application, which would extend beyond the expiration date of Application No. 11/821,221 has been reviewed and is accepted. The terminal disclaimer has been recorded. The obviousness double patenting rejection is hereby withdrawn.

Applicant's arguments have been fully considered but found not persuasive. The rejection(s) of the last Office Action are maintained for reasons of record and modified or repeated below for Applicant's convenience.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim(s) 28-29, 39-40 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, claim(s) 28-29, 39-40 recites the

limitation "said thiol-containing compound" in claims 21 and 32. There is insufficient antecedent basis for this limitation in the claims.

Response to Arguments

Applicant agrees that there is insufficient antecedent bases and do not contest this rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham vs John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim(s) 21-24, 28-29, 32-35, 39-40 are rejected under 35 U.S.C. 103(a) as being obvious over McCleary (US Patent Application 2002/0132219 A1) and Medford et al. (US Patent 5,750,351) in view of Applicant's admission of the prior art.

The instant claims are directed to a method for treating or normalizing hyperlipidemia and/or subcutaneous fat loss and body wasting resulting from anti-retroviral treatment of HIV-1 infection in a subject by administering triglyceride of conjugated linoleic acid and N-acetylcysteine.

McCleary teach a nutritional supplement composition comprising conjugated linoleic acid and the antioxidant, coenzyme Q10, for modulating nutrient partitioning in a human (abstract). Hyperlipidemia is disclosed as a disorder due to nutrient partitioning (section 0002). More particularly, it is desirable to provide a means for modulating aberrant pathways of nutrient partitioning so as to avoid excessive fat storage, to promote oxidation of fat, and reduce fat levels (sections 0006 to 0007). McCleary also discloses specifically triglyceride of conjugated linoleic acid (section 0010). McCleary also teach that fat synthesis and storage are diminished resulting in a fall in the intracellular fat content of the liver, pancreas, and skeletal muscle as well as a fall in visceral fat and total body fat stores accompanied by a decrease in individual fat cell volume (section 0023). Preferred amounts for CLA are 50 mg to 20 g and for alpha-lipoic acid are 25 mg to 2 g (Table 1).

Medford et al. teach that activation of the transcriptional regulatory factor, NF-kB, is linked to hyperlipidemia. Importantly, activation of NF-kB can be inhibited by antioxidants such as N-acetylcysteine (col. 2, lines 6-14).

It would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to have substituted coenzyme Q10 in the composition as taught by McCleary with N-acetylcysteine as taught by Medford.

A person of ordinary skill in the art would have been motivated to make this substitution because: (1) of the functional equivalence of both coenzyme Q10 and N-acetylcysteine as well-known antioxidants; and (2) both McCleary and Medford are aimed at treating hyperlipidemia. Therefore, one of ordinary skill in the art would have had a reasonable expectation of success in treating hyperlipidemia with a composition comprising a conjugated linoleic acid and the antioxidant, N-acetylcysteine.

However, McCleary and Medford fail to specifically disclose a patient population with hyperlipidemia coincident with subcutaneous fat loss and body wasting resulting from anti-retroviral treatment from an HIV-1 infection.

Applicant's disclosure of the prior art teaches that HIV infection is accompanied by disturbances in lipid and glucose metabolism. These metabolic abnormalities are further confounded by hypercholesterolemia and hypertriglyceridemia (both subgenus to hyperlipidemia) induced by anti-retroviral drugs. In fact, it is estimated that almost two-thirds of HIV/AIDS patients exhibit abnormal fat distribution coincident with AR-therapy. Clinicians have termed this abnormal fat distribution lipodystrophy or fat maldistribution, which describe the syndrome of body shape changes related to changes in fat distribution in people with HIV/AIDS receiving AR-therapy (section 0003 to 0009).

It is noted that the above paragraph describes the specific patient population that is claimed since abnormal fat maldistribution is defined as subcutaneous fat loss and body wasting resulting from anti-retroviral treatment from an HIV-1 infection.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to have administered a composition

comprising a conjugated linoleic acid and the antioxidant, N-acetylcysteine, as taught by McCleary and Medford to a patient with hyperlipidemia coincident with subcutaneous fat loss and body wasting resulting from anti-retroviral treatment from an HIV-1 infection.

A person of ordinary skill in the art would have been motivated to administer a composition comprising a conjugated linoleic acid and the antioxidant, N-acetylcysteine, as taught by McCleary and Medford to a patient with hyperlipidemia coincident with subcutaneous fat loss and body wasting resulting from anti-retroviral treatment from an HIV-1 infection because: (1) Applicant's admission of the prior art teaches that HIV infection is accompanied by disturbances in lipid and glucose metabolism and that these metabolic abnormalities are further confounded by hypercholesterolemia and hypertriglyceridemia (both subgenus to hyperlipidemia) induced by anti-retroviral drugs; and (2) Applicant's admission of the prior art teaches that it is estimated that almost two-thirds of HIV/AIDS patients exhibit abnormal fat maldistribution, which describe the syndrome of body shape changes related to changes in fat distribution in people with HIV/AIDS receiving AR-therapy. Therefore, one of ordinary skill in the art would have had a reasonable expectation of success in treating a patient with hyperlipidemia coincident with subcutaneous fat loss and body wasting resulting from anti-retroviral treatment from an HIV-1 infection by administering a composition comprising a conjugated linoleic acid and N-acetylcysteine.

Response to Arguments

Applicant argues that while Medford teach that activation of the transcriptional factor NF-kB is linked to hyperlipidemia, the linkage described by Medford is "causative" and not resultant. That is to say, Medford teach hyperlipidemia , in combination with other risk factors, such as smoking, may cause NF-kB activation resulting in atherosclerosis, but hyperlipidemia is not a result of NF-kB activation.

This is not persuasive because while Medford may or may not make the link between NF-kB and hyperlipidemia as causative, Medford does teach some link does exist. Applicant is reminded that the standard for obviousness is not absolute but a reasonable expectation of success.

Applicant argues against the teaching in Medford that activation of NF-kB can be inhibited by antioxidants, such as N-acetylcysteine. Applicant argues that the prior art had repeatedly demonstrated that inhibition was a function of the activator or stimulation used and that antioxidants were cell-specific in their ability to inhibit NF-kB activation.

This is not persuasive because the teaching by Medford that N-acetylcysteine inhibits NF-kB is from a valid issued US Patent. A patent shall be presumed valid. Each claim of a patent (whether in independent, dependent, or multiple dependent form) shall be presumed valid independently of the validity of other claims; dependent or multiple dependent claims shall be presumed valid even though dependent upon an invalid claim. The burden of establishing invalidity of a patent or any claim thereof shall rest on the party asserting such invalidity. *35 U.S.C. 282 Presumption of Validity*

Applicant argues the functional equivalence of both coenzyme Q10 and N-acetylcysteine as well known antioxidants. This assertion is based on differences in bioavailability, the location in cells, and the additional function as a pro-oxidant.

This is not persuasive because these assertions raised by the Applicant do not affect the functional properties of the antioxidants.

Applicant argues that both McCleary and Medford are not aimed at treating hyperlipidemia. While McCleary teaches a combination comprising CLA for the treatment of hyperlipidemia, at the time of the claimed invention seven of eight published clinical studies indicated a lack of effect of CLA on lowering blood lipids. Applicant continues to argue that Medford does not teach treating hyperlipidemia but rather atherosclerosis.

This is not persuasive because these clinical studies appear not to be conclusive because no long term studies were investigated. In fact, one of the seven appear to support the teachings of the McCleary reference. With regard to Medford, it is clear that both atherosclerosis and hyperlipidemia are contemplated by the teachings.

The Babish Declaration under 37 CFR 1.132 filed 10/27/08 is insufficient to overcome the rejection of claims 21-24, 28-29, 32-35, 39-40 based upon McCleary (US Patent Application 2002/0132219 A1) and Medford et al. (US Patent 5,750,351) in view of Applicant's admission of the prior art.

First of all, the Declaration seems make the case that the state of the art is that CLA or NAC is inoperable for decreasing blood lipids. This is not true because both McClearly and Medford in addition to the one prior art reference teach otherwise.

Therefore, a showing of seven of nine references do not constitute the state of the art in terms of being inoperable for decreasing blood lipids.

Secondly, the arguments directed to increasing insulin sensitivity do not apply here since the claimed invention is irrelevant to reducing side effects or increasing insulin sensitivity. The cited prior art references are valid and relevant as long as treating hyperlipidemia is taught, regardless of whether insulin sensitivity is increased or whether the formulation was safe or easily tolerated.

Thirdly, the claimed unexpected results are not unexpected because the cited prior art clearly teaches treating hyperlipidemia. The presented evidence merely shows that the claimed invention is enabled. There is nothing to show that the results are unexpected or synergistic. The teaching that the formulation is safe or well tolerated is not a showing of unexpected or synergistic results.

Lastly, there is no side by side comparison with the closest prior art. Furthermore, the results are not commensurate with the scope of the claims, especially since the data shows no dosage amounts, whereas the instant claims recite any and all dosages.

In view of the foregoing, when all of the evidence is considered, the totality of the rebuttal evidence of nonobviousness fails to outweigh the evidence of obviousness.

Regarding the establishment of unexpected results, a few notable principles are well settled. It is applicant's burden to explain any proffered data and establish how any results therein should be taken to be unexpected and significant. See MPEP 716.02 (b). The claims must be commensurate in scope with any evidence of unexpected

results. See MPEP 716.02 (d). Further, a DECLARATION UNDER 37 CFR 1.132 must compare the claimed subject matter with the closest prior art in order to be effective to rebut a prima facie case of obviousness. See MPEP 716.02 (e). Applicants fail to provide clear and convincing evidence to support the alleged unexpected benefit.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong S. Chong whose telephone number is (571)-272-8513. The examiner can normally be reached on M-F, 9-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SREENI PADMANABHAN can be reached on (571)-272-0629. The fax

phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Yong S. Chong/
Primary Examiner, Art Unit 1627

YSC